

Attorney Docket No. 6176.200-US  
Persson et al.

Serial No. 09/848,107

Filed May 3, 2001

### REMARKS

Reconsideration and allowance are respectfully requested.

Claims 1-13 and 24-28 were pending. In this response, claims 1, 11, and 12 are amended; claim 10 is cancelled, and new claims 30 and 31 have been added. Support for the amendments can be found in the original claims; no new matter is added. Accordingly, claims 1-9, 11-13, 24-28, 30, and 31 are pending and at issue.

Applicants thank the Examiner for the courtesies extended during an interview on November 3, 2004. It is believed that this amendment reflects the substance of the interview.

### Notice of Related Applications

The Examiner is informed of the following co-pending and commonly owned U.S. applications:

Application Serial No.	Filing Date
10/281,727	10/28/02
09/931,121	9/13/01
10/295,682	11/15/02
10/256,032	9/24/02
10/281,727	10/28/02
10/109,498	3/22/02
10/200,473	7/19/02
10/196,902	7/16/02

The Examiner is also informed of another patent application (not commonly assigned), serial number 10/415,963, filed May 5, 2003 (publication number 20040033566), directed to Factor VIIa variants. (This patent application publication is also cited in an Information Disclosure Statement being filed concurrently herewith.)

Attorney Docket No. 6176.200-US  
Persson et al.

Serial No. 09/848,107

Filed May 3, 2001

### **Restriction Requirement**

By presenting claims to a method of treating bleeding episodes, Applicants request that the Examiner, upon allowance of claims directed to Factor VII variants, re-join these claims and include them in the allowed claims.

### **Double Patenting**

Claims 1, 2, 7, 8, 10-13, 24-25, 27, and 28 have been provisionally rejected under the judicially created doctrine of obviousness-type double patenting over claims 1, 4, 6, and 7 of co-pending application serial no. 10/109,498 (the "'498 application"). A terminal disclaimer is appended herewith.

Claims 1, 2, 7, 8, 24, 25, 27, and 28 have been provisionally rejected under the judicially created doctrine of obviousness-type double patenting over claims 1, 4, 6, and 7 of co-pending application serial no. 10/281,727. A terminal disclaimer is appended herewith.

It is respectfully submitted that the terminal disclaimers overcome the double patenting rejections and that they should be withdrawn.

### **Rejection Under 35 U.S.C. § 102**

Claims 1, 7, 24, and 27 have been rejected under 35 U.S.C. § 102(e) as anticipated by Pedersen et al., US 2003/0096338 (US application serial no. 09/782,587, the "'587 application"). The Examiner contends that Pedersen et al. discloses L305 variants of Factor VIIa. This rejection is respectfully traversed.

The Pedersen et al. patent application claims priority from US provisional application serial no. 60/184,036 (the "'036 application"), filed February 22, 2000 and from US provisional application serial no. 60/241,916 (the "'916 application"), filed October 18, 2000 (after the US priority date of the present application, May 16, 2000.)

L305 is mentioned in the published '587 application as a target for mutation only in the context of engineering an additional glycosylation site. See, e.g., paragraph 126. Comparison of the '587 application with the '036 application failed to reveal a single mention of L305 as a target for mutation. Compare, e.g., paragraph 126 of the '587 application with the corresponding text in the '036 application at page 10, lines 17-29. The only mention of L305 in the '036 application occurs in Example 1, which lists it (along with 46 other residues) as being in the tissue factor-binding site of Factor VII; however, there is no hint or suggestion that it could be a target for mutation. Thus, the disclosure in Pedersen et al. of L305 as a target for mutation is not entitled to a February 22, 2000 102(e) date.

Attorney Docket No. 6176.200-US  
Persson et al.

Serial No. 09/848,107

Filed May 3, 2001

For these reasons, it is respectfully submitted that Pedersen et al. does not anticipate the present claims and that this rejection may be withdrawn.

**Rejection Under 35 U.S.C. § 103**

Claims 1, 2, 7, 8, 24, 25, 27, and 28 have been rejected under 35 U.S.C. § 103(a) as unpatentable over Dickinson et al., *Proc. Natl. Acad. Sci. USA* 93: 14379, 1996, further in view of Pedersen et al., the *Dictionary of Biochemistry and Molecular Biology*, and Berkner et al., U.S. Patent No. 5,288,629. The Examiner contends that Dickinson et al. discloses replacement of L305 with Ala; that Pedersen et al. discloses substitution of L305 with Asn; that the *Dictionary* defines conservative amino acid substitutions; that Berkner et al. discloses Factor VII variants having reduced proteolytic activity; and that it would have been obvious to combine the teachings in these references to achieve the present invention. This rejection is respectfully traversed.

The invention as presently claimed requires Factor VII variants that exhibit *increased* proteolytic activity relative to the parent enzyme, wild-type Factor VIIa.

As discussed above, Pedersen et al. is not a reference against the present claims.

Dickinson et al. describes a study in which individual amino acids within the Factor VII sequences were changed to alanine (so-called "ala scanning" technique). Dickinson et al. did not identify L305 as a residue that could be mutated in order to enhance proteolytic function. Furthermore, there is no hint or suggestion in Dickinson et al. of how to achieve such enhancement.

Neither the *Dictionary* nor Berkner et al. remedies the deficiencies of Dickinson et al. The general guidance of the *Dictionary* as to what does, or does not, constitute a conservative mutation would not assist in directing one of ordinary skill in the art to any particular residues with human Factor VII as targets for mutation, or, specifically, to indicate that L305 could be mutated so as to enhance proteolytic function. Berkner et al. is silent with respect to Factor VII variants having *increased* activity, but rather relates to variants having *reduced* activity.

Accordingly, none of the cited references, either singly or in combination, could have provided one of ordinary skill with any reasonable expectation of achieving the presently claimed Factor VII variants. On this basis, it is respectfully submitted that the present claims are non-obvious over the cited references and that this rejection should be overcome.

Attorney Docket No. 6176.200-US  
Persson et al.

Serial No. 09/848,107

Filed May 3, 2001

In view of the above response, it is respectfully submitted that the claims are in condition for allowance, and a determination to that effect is earnestly solicited.

Date: November 5, 2004

Respectfully submitted,



Reza Green, Reg. No. 38,475  
Novo Nordisk Pharmaceuticals, Inc.  
100 College Road West  
Princeton, NJ 08540  
(609) 987-5800

23650

PATENT TRADEMARK OFFICE